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Commission Workshop on a roadmap towards phasing out animal testing for chemicals safety

A national risk assessor's perspective to move towards the assessment of systemic health effects using non-animal methods

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Some Preliminary Statements

Our ultimate goal is to ensure a safe use of chemicals with a sufficient level of confidence:

- By doing evidence- based risk assessment for general population, workers and the Environnement,
- By complying with the regulatory framework
- With available resources
- With only well justified use of animals

ANSES has several key roles:

ANSES as a regulatory risk assessment Agency

CLP
REACh
Pesticides,
Vet. Drugs
Biocides
https://www.anses.fr/en

ANSES being a major research player

ANSES is coordinating PARC
https://www.eu-parc.eu/

ANSES part of broad network at international, EU and national levels

Involved in
ECHA, EFSA, EMA,
OECD, WHO…

So far, where are we with NAMs?

- Still limited use when we have to respond to regulatory mandates
- NAMs are not available yet to fulfil most of the obligations related to Information Requirements
- Can only replace animals if allowed by sectorial regulations, eg REACH article 13:

NAMs should be employed based on requirements outlined in Annex XI section 1, including:

- that results are derived from NAMs methods that meet scientific validation requirements:
  → acceptance of the data;
- that the NAM is fit for the purpose specified:

  → able to inform on hazard and risk
- that adequate documentation for the NAM is available

→ clear view on reproducibility, sensitivity, specificity and applicability domain

In practice, NAM can be used to justify proper read-across if this allow hazard identification and risk assessment

But our experience on how registrants or applicants use these opportunities to reduce animal testing is rarely satisfactory

So far, where are we with NAMs ?

For risk assessment of regulated substances

Exposure Assessment	Hazard Assessment	Uses of NAMs for Exposure	Uses of NAMs for Hazard for systemic effects in Human
• Possible only when exposure is voluntary/ defined or known • For most of chemicals uses, we miss data on uses and exposure • Modeling often not transparent or well justified	• CLP classifications rely on Human or Animal evidence • Information Requirement mainly based on *in vivo* data • When NAMs are used to waive animal testing , very often not well justified in the dossiers	• *In vitro* data for Toxico kinetics • *In vitro* Metabolism • *In vitro* skin penetrations studies • Exposure models (Consexpo…)	• Limited for pesticides and biocides • Already possible in Reach when scientifically robust • Until robust should not be used to justify a waiving • new animal studies not possible for cosmetics

Reg. bodies need to be able to assess

Still very limited

Prerequisites before shifting from animals to NAMs

1. Validation

- Mutual Acceptance of Data
- Regulatory readiness
- Inclusion in OECD test guidelines
- Valid (and not always "validated") methods
- Not only methods should be valid but also models, tools …

2. Human / other species Relevance

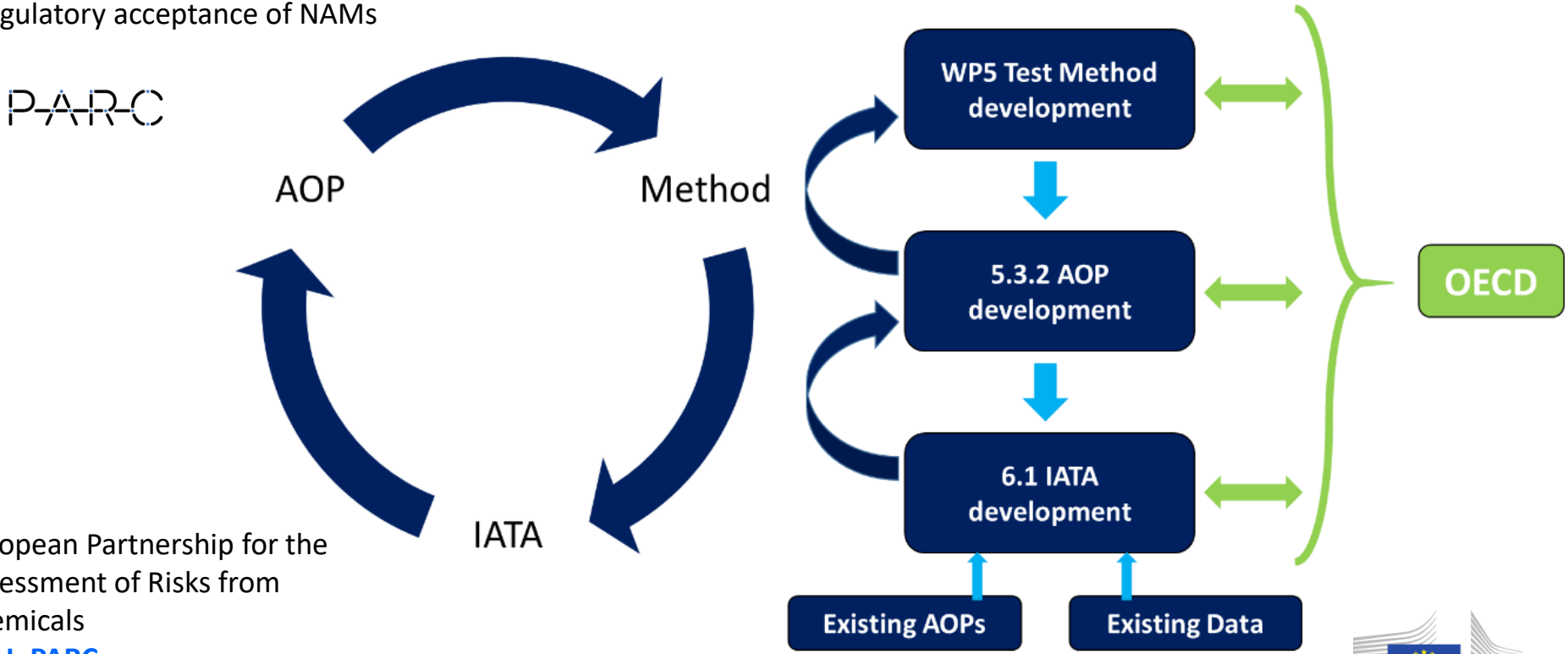
- Comparison between *in vitro* and *in vivo* still needed: sensitivity and applicability domain
- Good positive and negative controls
- Demonstration of the relevance of the *in vitro* models for Human/ other species toxicity
- Demonstration of the sensitivity and specificity of the methods for environmental level of exposure

3. Access to data

- All data should be made fairly accessible to regulatory risk assessors
- Battery of tests with clear interpretation → guidelines
- Need for endorsed Adverse Outcome Pathways (AOPs)
- Need for recognized Test Strategies for Hazard and Risk Assessment (IATAs)

Prerequisites before shifting from animals to NAMs

There are scientific activities with PARC (specifically in WP5 and WP6) that may contribute to the validation and regulatory acceptance of NAMs



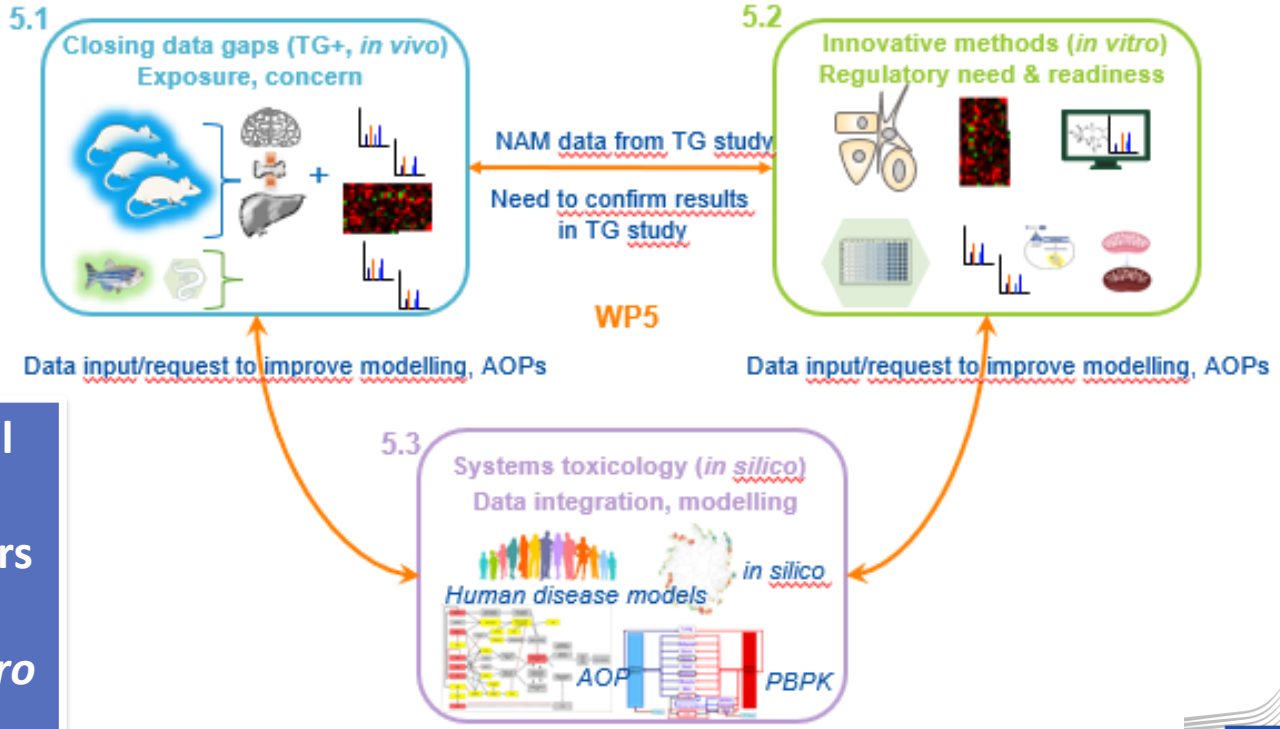
European Partnership for the Assessment of Risks from Chemicals

#EU_PARC

WP5: **Hazard Assessment** **BfR(DE) and ANSES (FR)**

WP6: **Innovation in Regulatory Risk assessment** **KEMI (SE) and RIVM (NL)**

General Approach on Hazard Assessment : PARC- WP5



We still need animal data with more sensitive parameters (eg. omics) to compare with *in vitro* methods

WP5: **Hazard Assessment** BfR(DE) and ANSES (FR)

Prerequisites before shifting from animals to NAMs: Enrich the ECHA database

How:

- Ensure good quality animal tests with controlled reporting (thesaurus):
  - Tests with additionnal environmental doses (additionnal cost to be aknowledged)
  - Include sensitive methods, biomarkers, early events
  - Gather the study reports instead of RSS

- If NAMs are requested @annex VII, get **animal testing as trigger** or @ annexes >VII:
  - define the sensitivity/ specificity and applicability domain in life-size comparisons

- Get access to data from pharma industry to have gold-standards:
  - NAM development and data on specific chemicals

Prerequisites before shifting from animals to NAMs: Enrich the ECHA database

Why:

- Get acceptance and train the assessors:
  - Avoid the black-box effect
  - Define ahead how to design the regulations: integration of proper Integrated Testing Srtategies and to ensure the regulatory bodies to be able to assess

- Mine the data (existing and to be gathered) to detect signals and alerts:
  - Will help to design fit for purpose NAMs

- Populate the database to be able to rely on an AI-tool able to assess future new chemicals without animals **whatever the applicability domains**

What can we do now ?

Proactive positioning strategy

Anses is already using NAMs instead of animal data whenever possible :

- **To classify compounds,** but in practice, data (often *in vivo*) are necessary for RAC (ECHA Committee for Risk Assessment) to accept read-across for systemic effects

  → the weight of evidence to justify Read-Across needs to be very strongly justified

If we want to include NAMs in chemical regulations, we first need to include them in CLP, then Information requirements could be adapted accordingly

- **To prioritize compounds for further works (eg. endocrine active substances)**

Anses is also supporting research activities within this field:

- Active participation of ANSES teams in European research projects and partnerships

PARC, PEPPER Platform, National Research Programmes….

Horizon 2020 / Horizon Europe

During the transition period

- Share Data: Transparency!
- Use of NAMs based on the level of confidence we have
- Avoid replication of animal Testing! “One substance One Registration” has been very efficient: carry on with “One substance One Assessment” approach
- Better knowledge about chemically induced human diseases (and biodiversity loss)
- Training of Risk Assessors: create NAM-WG @ ECHA
- Cases studies to increase confidence in the use of NAMs in a regulatory context

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Thank you for your attention!